

**Exhibit A**  
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**1. Service Overview**

Vendor agrees to provide to the State of California Department of Public Health (CDPH), Genetic Disease Screening Program (GDSP) the services described herein.

The purpose of the vendor agreement is to provide confirmatory testing of infants with Newborn Screening (NBS) results that are positive for a potentially significant hemoglobinopathy. Confirmatory testing includes testing the parents whose results are necessary to confirm the infant's NBS results.

**2. Service Location**

The services shall be performed at:

5700 Martin Luther King Jr. Way  
Oakland, CA 94609-1673.

**3. Service Hours**

The services shall be provided during normal Vendor working hours, but at a minimum of Monday through Friday, 8:00 am – 5:00 pm, excluding state holidays.

**4. Project Representatives**

A. The project representatives during the term of this vendor agreement will be:

<b>California Department of Public Health</b>  Administrator  Muslimah Jaavaid Telephone: (510) 412-1476 Fax: (510) 620-6258 Email: <a href="mailto:M.Jaavaid@cdph.ca.gov">M.Jaavaid@cdph.ca.gov</a>	<b>Children's Hospital &amp; Research Center at Oakland</b>  Project Director: Bertram Lubin, MD, President and CEO 5700 Martin Luther King Jr. Way Oakland, CA 94609-1673 Telephone: (510) 450-7600 Fax: (510) 450-7910 Email: <a href="mailto:BLubin@mail.cho.org">BLubin@mail.cho.org</a>
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B. Direct all inquiries to:

<b>California Department of Public Health</b> NBSP Hemoglobin Reference Lab Vendor Liaison: Genetic Disease Screening Program Attention: Shellye Lessing, MS 850 Marina Bay Parkway, F175, MS 8200 Telephone: (510) 412-1487 Fax : (510) 412-1552 Email : <a href="mailto:Shellye.Lessing@cdph.ca.gov">Shellye.Lessing@cdph.ca.gov</a>	<b>Children's Hospital &amp; Research Center at Oakland</b>  Contract Manager: Rebecca Rosales 5700 Martin Luther King Jr. Way Oakland, CA 94609-1673 Telephone: (510) 450-7698 Fax: (510) 450-7973 Email: <a href="mailto:Rrosales@chori.org">Rrosales@chori.org</a>
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- C. Either party may make changes to the information above by giving written notice to the other party within 30 days of the anticipated change. Said changes shall not require an amendment to this vendor agreement.

**5. Services to be Performed**

The Vendor shall perform the following services:

**A. Confirmatory Testing for Hemoglobin Disease Positive Newborn Screening Results**

As a hemoglobin confirmatory laboratory for follow-up of initial positive screening results consistent with a potentially clinically significant hemoglobin disorder, the Vendor shall provide CDPH with hemoglobin confirmatory testing on blood specimens from infants born in California whose screening results are defined as indicative of a potentially significant hemoglobinopathy; and on blood specimens from the parents of newborns, whose results are necessary to confirm the screening results. Initial NBS positive results include but are not limited to hemoglobin patterns of F, FS, FSa, FSC, FSD, FSE, FSV, where V means an unknown variant hemoglobin, FE, FV, FC, FCa, FD, FDa, FEa; patterns with four hemoglobins if A is absent; patterns including an amount of Hb Barts above the cutoff for Hemoglobin H disease; and newborns who were transfused prior to NBS collection who have a hemoglobin pattern containing one or more hemoglobin variants.

1. Provide the Newborn Screening Program Area Service Centers (ASCs) with instructions for proper collection of hemoglobin confirmatory specimens.
2. Receive specimens from ASCs, newborn's physician, hospital, or California Children's Services (CCS)-approved Sickle Cell Disease Centers. Notify the ASC of receipt of specimens.
3. Analyze hemoglobin confirmatory specimens within ten (10) working days of receipt using the following methods:
  - a. Separation of hemoglobins F, A, S, C, D and E with relative concentrations for each hemoglobin on all specimens by cellulose acetate-citrate agar electrophoresis, isoelectric focusing, high pressure liquid chromatography, and/or DNA analysis as approved by the CDPH.
  - b. Provide a hemogram on each suitable specimen to include hemoglobin, red blood cell count (RBC), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and red cell distribution width (RDW).
  - c. Perform Free Erythrocyte Protoporphyrin (FEP) on specimens with microcytic hypochromic anemia.
  - d. Provide quantitative hemoglobin A2 when necessary to resolve phenotype.

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- e. Provide quantitative hemoglobin F when necessary to resolve phenotype.
4. Provide DNA analysis to differentiate between EE and E/Beta thalassemia, to detect beta thalassemia mutations in newborns with results of FS, FC, or FD in the absence of one parent, to identify the beta thalassemia mutation in the infant when one parent has elevated Hb A2, and to examine inconsistencies between thin layer isoelectric focusing profiles of newborn and parents. Provide beta globin DNA analysis for infants with an NBS pattern of "FSa", "FCa", "FDa" and "FEa" to confirm a beta+ thalassemia mutation.
5. Provide CDPH with DNA analysis for alpha globin deletions and other point mutations on samples from infants with Barts Hb above the cutoff for Hb H disease on the NBS within fifteen (15) business days of receipt of specimen.
6. Provide CDPH with analysis for unusual Hb variants such as: Hb Korle Bu, HB T Cambodian, Hb Matsue-Okii, Hb O Arab, Hb C Harlem, Hb G Philadelphia, Hb Constant Spring carried in compound heterozygosity with clinically significant hemoglobin variants (including but not limited to Hb S, C, E mutations, beta thalassemia, or Hb Barts) or as only the adult hemoglobin (FV pattern). DNA studies for Hb Constant Spring will be completed within fifteen (15) business days of receipt of specimen. Presumptive findings for and the presumptive diagnosis for Hb Korle Bu, HB T Cambodian, Hb Matsue-Okii, Hb O Arab, Hb C Harlem, Hb G Philadelphia will be completed and reported within thirty (30) days, and final determination within ninety (90) days of receipt of specimen. Any deviations in timeframe will be reported and explained to the CDPH.
7. Provide CDPH with analysis of unknown rare variants carried in compound heterozygosity with clinically significant hemoglobin variants (including but not limited to Hb S, C, E mutations, beta thalassemia, or Hb Barts) or as only the adult hemoglobin within ninety days (90) days of receipt of specimen.
8. Report initial and any subsequent test results to the ASC and to Genetic Disease Screening Program (GDSP) within twenty-four (24) hours of completion of the test; enter test result into the GDSP's internet-based computerized Screening Information System (SIS). Provide a written report of test results, interpretations of results and recommendations for follow-up to the ASC with a copy to GDSP. The test results report must list the telephone number at which physicians can obtain hematological consultation. The report of test results must be typewritten with no handwritten notes or crossed out words. If a report subsequently requires an amendment or correction, a new report will be issued and labeled as amended or corrected. A dated addendum may be added to the initial report. Additional or new interpretation or recommendations must be reviewed, signed and dated by the hematologist.
9. The Vendor shall provide consultation upon request to referring physicians, to ASCs and Newborn Screening Branch (NBSB) staff regarding interpretations of laboratory data, family history or other information necessary to provide accurate diagnosis or

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reproductive risk counseling to families referred as a result of the California Newborn Screening Program.

10. Test hemoglobin confirmatory specimens using the tests, including DNA analyses, which, after consultation with newborn's physicians or the Medical Director of the ASC, are determined necessary for accurate counseling.
11. Reports on patterns containing a hemoglobin variant(s) must state when a final determination will be completed, not to exceed ninety (90) days from receipt of specimen. Interim or incomplete information on the variant(s) should be reported if known.
12. Recommend additional appropriate laboratory tests necessary for accurate counseling or diagnosis.

**B. Follow-up Testing for Hemoglobin Results of Unknown Significance on Newborn Screening (Follow-up requested by primary care provider)**

As a hemoglobin consultation laboratory, Vendor shall provide, after appropriate consultation with newborn's physician, any tests on specimens from newborns or their families where additional testing is authorized by the CDPH based on unusual newborn screening patterns, including, but not limited to FCD, FCE, FCV, FDC, FDE, FDV, FEC, FED, FEV, FVC, FVD, FVE, FVV; patterns of four hemoglobins with A present, newborns transfused prior to screening, and patterns of FAV or FVA.

**C. Follow-up Testing for Families of Newborns with Hb S, C, or D Trait**

As a hemoglobin reference laboratory for hemoglobin carrier trait follow-up, Vendor shall provide CDPH with hemoglobin testing on blood specimens from families of newborns born in California whose screening results have been defined by CDPH as carriers of sickling and other specific hemoglobins. These patterns include, but are not limited to FAS, FAC, FAD, FSA, FCA, FDA, and results of AFS, AFC or AFD in older babies. Vendor shall provide testing to parents, siblings and other family members of the screened newborn upon receipt of blood samples submitted by the newborn's physician, hospital, outpatient lab, CCS-approved Sickle Cell Disease Center or Sickle Cell Trait Follow-up Program-contracted phlebotomy sites accompanied by a Newborn Screening Hemoglobin Trait Lab Intake form. If a confirmatory specimen is submitted on the newborn it shall also be tested.

1. Provide the NBS Sickle Cell Trait Counselor or other sites at the request of the counselor with instructions for proper collection of hemoglobin confirmatory specimens.
2. Receive specimens from the newborn's physician, hospital or outpatient lab, Sickle Cell Trait Follow-up Program-contracted phlebotomy sites or CCS-approved Sickle Cell Disease Center.
3. Analyze specimens referred as part of carrier trait follow-up within ten (10) working days of receipt using the following methods:

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- a. Separation of hemoglobins F, A, S, C, D, and E with relative concentrations for each hemoglobin on all specimens by cellulose acetate-citrate agar electrophoresis, isoelectric focusing, high pressure liquid chromatography, and/or DNA analysis as approved by the CDPH.
  - b. Provide a hemogram on each suitable specimen, to include hemoglobin, hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and red cell distribution width (RDW).
  - c. Perform Free Erythrocyte Protoporphyrin (FEP) on specimens with microcytic hypochromic anemia.
  - d. Provide quantitative hemoglobin A2 when necessary to resolve phenotype or genotype.
  - e. Provide quantitative hemoglobin F when necessary to resolve phenotype or genotype.
  - f. Provide DNA analysis when necessary to resolve phenotype or genotype.
4. Report test results to the NBS Sickle Cell Trait Counselor at the GDSP within twenty-four (24) hours of completion of the test; enter test results into the GDSP's Screening Information System (SIS) program. Provide a faxed copy of the written report of test results, interpretations of results and recommendations for follow-up to the GDSP and hard copies of the reports to the Sickle Cell Trait Follow-up Program Coordinator. The test results report must list the telephone number at which physicians can obtain hematological consultation. The report of test results must be typewritten with no handwritten notes or crossed out words. If a report subsequently requires an amendment or correction, a new report will be issued and labeled as amended or corrected. A dated addendum may be added to the initial report. Additional or new interpretation or recommendations must be reviewed, signed and dated by the hematologist.
  5. Provide the NBS Sickle Cell Trait Counselor at the GDSP with analysis of an unknown rare variant trait in a parent when the other parent is a carrier of a clinically significant hemoglobin variant (including but not limited to Hb S, C, E mutations, beta thalassemia, alpha thalassemia or an unknown variant) within ninety days (90) days of receipt of specimen.
  6. Reports on patterns containing a hemoglobin variant(s) must state when a final determination will be completed, not to exceed ninety (90) days from receipt of specimen. Interim or incomplete information on the variant(s) will be reported if known in writing within thirty (30) days of receipt of specimen.
  7. The Vendor shall also provide consultation upon request to the newborn's physician, Sickle Cell Trait Counselor and Newborn Screening Branch staff regarding

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interpretations of laboratory data, family history or other information necessary to provide accurate diagnosis or reproductive risk counseling to families referred as a result of the California Newborn Screening Program.

8. Recommend additional appropriate laboratory tests necessary for accurate counseling or diagnosis.
  9. Test hemoglobin confirmatory specimens using the tests including DNA analyses which, after consultation with newborn's physician or consulting hematologist are determined necessary for accurate counseling.
- D. Vendor shall perform such laboratory services according to the vendor agreement at the location named on the Vendor's current State of California clinical license, unless the CDPH approves a subcontract for a portion of the testing. Consultation to providers or testing for hemoglobin specimens other than those specifically authorized by the CDPH is not covered or reimbursed by this vendor agreement.
- E. Vendor shall conduct analyses following methods approved by the Genetic Disease Laboratory Branch (GDLB). Each method shall contain a quality control program including, but not limited to the following elements:
1. Identification of calibrators and quality control reference samples by matrix and content.
  2. Placement of calibrators and quality control reference samples in each analytical run.
  3. Directions for use of calibrators in assignment of patient sample results.
  4. Instructions for interpretation of quality control results with reference samples and definition of parameters for acceptable analytical runs.
  5. Procedure for review of quality control results by the person responsible for releasing results.
  6. Definition of actions for unacceptable analytical runs, including not reporting results until those results are obtained in an analytical run that is within quality control parameters.
  7. Method for recording quality control results.

The Vendor agrees to make changes in the methods which CDPH judges to be in the best interests of the statewide newborn screening program; such changes may include items such as the amount of blood collected for testing, additional quality control actions and standardization of methods.

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- F. The Vendor shall provide all staff, equipment items, reagents, and consumables necessary for tests covered by the vendor agreement.
- G. The Vendor shall report inadequate specimens by telephone to the ASC, Newborn Screening Sickle Cell Trait Counselor, newborn's physician or CCS-approved Sickle Cell Disease Center requesting the test on the day of receipt within normal working hours so that an adequate repeat specimen can be obtained.
- H. If a specimen is mislabeled, inaccurately tested, damaged or lost, the Vendor must notify the ASC or Newborn Screening Sickle Cell Trait Counselor at the GDSP immediately by telephone so that an adequate repeat specimen can be obtained.
- I. The Vendor shall store specimens that remain after testing for at least thirty (30) days in a manner that preserves the integrity of the specimen. Any hemoglobin specimens transported to CDPH at CDPH request shall be transported at CDPH expense.
- J. All specimens sent for confirmatory testing for hemoglobinopathies identified in the California Newborn Screening Program, or for testing of family members of infants identified with a hemoglobin trait in the newborn screening program are the property of the State of California. The specimens cannot be used for additional testing beyond the scope of this vendor agreement for hemoglobin diagnosis without prior written permission from the GDSP.
- K. The Vendor shall subscribe to available proficiency testing programs applicable to hemoglobin test methods and shall send copies of performance reports to CDPH GDLB immediately following the receipt by the Vendor.
- L. The Vendor shall retain all laboratory records for a minimum of three (3) years following the end of the vendor agreement and make them available to CDPH staff or agents upon request.
- M. The Vendor shall provide quarterly summary reports to CDPH GDSP in a manner designated by GDSP.
- N. The Vendor shall have on site as a member of the staff of the Reference Laboratory a California licensed physician with expertise in the diagnosis of hemoglobinopathies. This expertise is demonstrated by specialty boards in hematology and by publications on the subject within the last five (5) years in accepted medical literature with peer review. Additionally, she/he shall have agreed in writing to perform all interpretations and recommendations for the Reference Laboratory and be available on site on a daily basis during normal business hours to initiate consultation on appropriate testing or counseling. The person who shall provide these services is designated as Consulting Hematologist.
- O. The Vendor shall be subject to on site inspections by CDPH GDLB and NBSB. The Vendor shall be subject to continuous contact and consultation by CDPH including review of data and records, and modification of items in the Vendor's methods,

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procedures and any other Reference Laboratory function.

- P. The Vendor shall not release, publish, put on a website, or otherwise distribute without prior written authorization from the CDPH GDSP vendor agreement liaison information acquired as a result of this work, including data, records, and information pertinent to the California Newborn Screening Program, the ASCs, the Hemoglobin Reference Laboratory or CCS-approved Sickle Cell Disease Centers.

**6. Reimbursement**

The GDSP shall reimburse the Vendor using a unit-cost methodology for services listed in Exhibit B – Vendor Payment Provision. See Exhibit B for a detailed outline of the rate schedule. The Vendor may submit itemized invoices to the GDSP for reimbursement on a quarterly basis.