**SUPPLEMENTAL MATERIAL**

**Sample Quality Assurance and Laboratory Proficiency (Approved July 2011)**

***Pre-Characterized Samples DNA Polymorphism Discovery Resource:*** To ensure genotyping proficiency of laboratories genotyping NBDPS buccal-derived DNA specimens independent of source material, the laboratories annually genotype a standard SNP set on a subset of the Coriell Institute for Medical Research’s Polymorphism Discovery Resource (PDR) DNA samples1. The SNP set is determined by the Genetic Analysis Working Group of the NBDPS and includes SNPs assayed by multiple labs and at least one SNP with publicly available genotypes on Coriell’s PDR samples. Standard 96 well plates that include 86 PDR samples, 4 replicates, 2 negative controls, and 4 empty wells for internal laboratory genotyping controls are plated by Coriell and sent directly to each laboratory. Plate formats and content are changed yearly. Laboratories are blinded to sample type and report genotyping results centrally to the Centers for Disease Control and Prevention for analysis. Since implementation of annual external quality assessment, call rates of 97-100% have been reported across NBDPS genotyping labs. Concordance rates of 99-100% have been reported between NBDPS labs and between NBDPS labs and the publicly available Coriell PDR genotypes. Due to higher costs, laboratories using higher throughput genotyping methods do not complete this annual assessment; instead, they complete an assessment using blood-buccal trio samples.

***Blood-Buccal Trios:*** To assure data quality across laboratories genotyping NBDPS buccal-derived DNA specimens, 36 blinded specimens ascertained through the University of Washington under an IRB-approved protocol and 2 DNA-negative controls are sent to each laboratory annually. The 36 specimens are comprised of paired cytobrush buccal and whole blood derived (gold standard) DNAs from 6 parent-offspring trios. The NBDPS Central Laboratory extracted buccal-derived DNAs using phenol chloroform, whole blood-derived DNAs using Gentra Puregene, quantified DNAs using RNaseP real-time quantitative PCR, and verified Mendelian inheritance using a microsatellite panel. Specimens were genotyped at each NBDPS genotyping laboratory for the standard SNP panel *both before and after whole genome amplification (WGA) (include last part of sentence if WGA)*. Due to higher costs, laboratories using higher throughput genotyping methods complete this assessment using 6 blinded specimens from 1 parent-offspring trio prior to initiating each project. Since implementation of external quality assessment, call rates of 92-100% have been reported across NBDPS genotyping labs. Concordance rates between paired blood-buccal samples were 100% *pre and post WGA*. Inter-laboratory concordance rates for variants assayed in common were 100%. Additionally, SNP genotyping was consistent with Mendelian inheritance.

**References**

1 Collins FS, Brooks LD, Chakravarti A. A DNA Polymorphism Discovery Resource for Research on Human Genetic Variation. Genome Res 1998;8: 1229-1231.